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NEWS 3 FEB 27
                 New STN AnaVist pricing effective March 1, 2006
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                 CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS 5 MAY 11
                 KOREAPAT updates resume
NEWS 6 MAY 19
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                 IPC 8 Rolled-up Core codes added to CA/CAplus and
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        MAY 30
                 USPATFULL/USPAT2
NEWS
        MAY 30
                 The F-Term thesaurus is now available in CA/CAplus
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         JUN 02
                 The first reclassification of IPC codes now complete in
                 INPADOC
NEWS 10
         JUN 26
                 TULSA/TULSA2 reloaded and enhanced with new search and
                 and display fields
NEWS 11.
         JUN 28
                 Price changes in full-text patent databases EPFULL and PCTFULL
         JUl 11
NEWS 12
                 CHEMSAFE reloaded and enhanced
         JUl 14
NEWS 13
                 FSTA enhanced with Japanese patents
         JUl 19
NEWS 14
                 Coverage of Research Disclosure reinstated in DWPI
NEWS 15
         AUG 09
                 INSPEC enhanced with 1898-1968 archive
NEWS 16
        AUG 28
                 ADISCTI Reloaded and Enhanced
NEWS 17
         AUG 30
                 CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 18
         SEP 11
                 CA/CAplus enhanced with more pre-1907 records
                 CA/CAplus fields enhanced with simultaneous left and right
NEWS 19
         SEP 21
                 truncation
                 CA(SM)/CAplus(SM) display of CA Lexicon enhanced
         SEP 25
NEWS 20
         SEP 25
NEWS 21
                 CAS REGISTRY(SM) no longer includes Concord 3D coordinates
         SEP 25
NEWS 22
                 CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 23
         SEP 28
                 CEABA-VTB classification code fields reloaded with new
                 classification scheme
NEWS EXPRESS
              JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
              MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.
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              STN Operating Hours Plus Help Desk Availability
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              For general information regarding STN implementation of IPC 8
NEWS X25
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FILE 'HOME' ENTERED AT 11:01:59 ON 02 OCT 2006

=> file pctfull

COST IN U.S. DOLLARS

SINCE FILE TOTAL

SESSION

FULL ESTIMATED COST

ENTRY 0.21 0.21

FILE 'PCTFULL' ENTERED AT 11:02:11 ON 02 OCT 2006 COPYRIGHT (C) 2006 Univentio

FILE LAST UPDATED:

25 SEP 2006

<20060925/UP>

MOST RECENT UPDATE WEEK:

200638

<200638/EW>

FILE COVERS 1978 TO DATE

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http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE (last updated April 10, 2006) <<<

>>> NEW PRICES IN PCTFULL AS OF 01 JULY 2006. FOR DETAILS, PLEASE SEE HELP COST <<<

=> s NGR

457 NGR

8 NGRS

L1458 NGR

(NGR OR NGRS)

=> s galactose

15757 GALACTOSE

184 GALACTOSES

L2 15772 GALACTOSE

(GALACTOSE OR GALACTOSES)

=> s 11 and 12

56 L1 AND L2

=> s 1 () 3 () galactos?

1058914 1

1041470 3

38133 GALACTOS?

379 1 (W) 3 (W) GALACTOS?

=> s 14 and 11

8 L4 AND L1

=> s 15 not py>2003

337448 PY>2003

6 L5 NOT PY>2003 L6

=> d ibib 1-6

ANSWER 1 OF 6

ACCESSION NUMBER:

PCTFULL COPYRIGHT 2006 Univentio on STN 2003063593 PCTFULL ED 20030818 EW 200332 METHODS FOR TREATING CANCER BY ADMINISTERING

TITLE (ENGLISH):

TUMOR-TARGETTED BACTERIA AND AN IMMUNOMODULATORY AGENT

METHODES DE TRAITEMENT DU CANCER PAR ADMINISTRATION D'UNE BACTERIE CIBLEE SUR UNE TUMEUR ET D'UN AGENT

IMMUNOMODULATEUR

TITLE (FRENCH):

INVENTOR(S): KING, Ivan, C., 65 Blue Hills Road, North Haven, CT 06473, US [US, US]; ZHANG, Li-mou, 406 Hilltop Road, Orange, CT 06477, US [US, US] PATENT ASSIGNEE(S): VION PHARMACEUTICALS, INC., Four Science Park, New Athens, CT 06511, US [US, US], for all designates States except US; KING, Ivan, C., 65 Blue Hills Road, North Haven, CT 06473, US [US, US], for US only; ZHANG, Li-mou, 406 Hilltop Road, Orange, CT 06477, US [US, US], for US only AGENT: BALDWIN, Geraldine, F.\$, Pennie & Edmonds LLP, 1155 Avenue of the Americas, New York, NY 10036\$, US English LANGUAGE OF FILING: LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE -----WO 2003063593 A1 20030807 DESIGNATED STATES W:AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW RW (ARIPO): RW (EAPO): AM AZ BY KG KZ MD RU TJ TM RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT SE SI SK TR RW (OAPI):
APPLICATION INFO.: BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG WO 2003-US2451 A 20030128 PRIORITY INFO.: US 2002-60/352,259 20020128 ANSWER 2 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN 1.6 ACCESSION NUMBER: 2003003906 PCTFULL ED 20030122 EW 200303 TITLE (ENGLISH): METHODS OF DIAGNOSIS OF BLADDER CANCER, COMPOSITIONS AND METHODS OF SCREENING FOR MODULATORS OF BLADDER CANCER TITLE (FRENCH): PROCEDE DE DIAGNOSTIC DU CANCER DE LA VESSIE, COMPOSITIONS ET PROCEDES DE CRIBLAGE DE MODULATEURS DU CANCER DE LA VESSIE INVENTOR(S): MACK, David, H., 2076 Monterey Avenue, Menlo Park, CA 94025, US; AZIZ, Natasha, 411 California Avenue, Palo Alto, CA 94306, US PATENT ASSIGNEE(S): EOS BIOTECHNOLOGY, INC., 225A Gateway Boulevard, South San Francisco, CA 94080, US [US, US] PARENT, Annette, S.\$, Townsend and Townsend and Crew AGENT: LLP, Two Embarcadero Center, Eighth Floor, San Francisco, CA 94111\$, US LANGUAGE OF FILING: English LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE -----WO 2003003906 A2 20030116 DESIGNATED STATES W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI

SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

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RW (EAPO):
RW (EAPO):
AM AZ BY KG KZ MD RU TJ TM
RW (EPO):
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC
NL PT SE SK TR
RW (OAPI):
BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.:
WO 2002-US21338
PRIORITY INFO.:
US 2001-60/302,814
20010703
US 2001-60/310,099
20010803
US 2001-60/350,666
20011113
US 2002-60/372,246
20020412
L6 ANSWER 3 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 2001025399 PCTFULL ED 20020820

TITLE (ENGLISH): NON-INVASIVE TUMOR IMAGING BY TUMOR-TARGETED BACTERIA

TITLE (FRENCH): IMAGERIE NON INVASIVE DE TUMEURS PAR DES BACTERIES
TITLE (FRENCH):
                          IMAGERIE NON INVASIVE DE TUMEURS PAR DES BACTERIES
                            CIBLEES SUR DES TUMEURS
INVENTOR(S):
                            BERMUDES, David, G.;
                            KING, Ivan, Cheung-Lam;
                            BLASBERG, Ronald, G.;
                            TJUVAJEV, Juri, G.
                            VION PHARMACEUTICALS, INC.;
PATENT ASSIGNEE(S):
                            SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH
DOCUMENT TYPE:
                            Patent
PATENT INFORMATION:
                            NUMBER KIND DATE
                            ______
                            WO 2001025399 A2 20010412
DESIGNATED STATES
                            AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
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                            CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
                            IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
                            MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
                            TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL
                            SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE
                            DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI
                            CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:
                           WO 2000-US27397 A 20001004
PRIORITY INFO.:
                           US 1999-60/157,620
                                                       19991004
        ANSWER 4 OF 6
                           PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:
                           2001025397 PCTFULL ED 20020820
TITLE (ENGLISH):
                           COMPOSITIONS AND METHODS FOR TUMOR-TARGETED DELIVERY OF
                          EFFECTOR MOLECULES
                           COMPOSITIONS ET METHODES D'ADMINISTRATION CIBLEES SUR
TITLE (FRENCH):
                            LES TUMEURS DE MOLECULES EFFECTRICES
                            BERMUDES, David, G.;
INVENTOR(S):
                            KING, Ivan, C.;
                            CLAIRMONT, Caroline, A.;
                            LIN, Stanley, L.;
                            BELCOURT, Michael
PATENT ASSIGNEE(S):
                            VION PHARMACEUTICALS, INC.;
                            BERMUDES, David, G.;
                            KING, Ivan, C.;
                            CLAIRMONT, Caroline, A.;
                            LIN, Stanley, L.;
                            BELCOURT, Michael
DOCUMENT TYPE:
                            Patent
PATENT INFORMATION:
                            NUMBER KIND DATE
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                            WO 2001025397 A2 20010412
DESIGNATED STATES
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TITLE (ENGLISH): METHODS FOR TREATING SOLID TUMORS WITH IRRADIATION AND METHODES DE TRAITEMENT DE TUMEURS SOLIDES PAR IRRADIATION ET BACTERIES BERMUDES, David, G.; LOW, Kenneth, Brooks; PAWELEK, John, M. VION PHARMACEUTICALS, INC.; YALE UNIVERSITY Patent NUMBER KIND DATE WO 2001024637 A1 20010412 AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG WO 2000-US27391 A 20001004 US 1999-60/157,621 19991004 PCTFULL COPYRIGHT 2006 Univentio on STN ACCESSION NUMBER: 2001014579 PCTFULL ED 20020828 COMPOSITIONS AND METHODS FOR DELIVERY OF AN AGENT USING ATTENUATED SALMONELLA CONTAINING PHAGE COMPOSITIONS ET PROCEDES POUR LA DELIVRANCE D'UN AGENT PAR LE BIAIS D'UNE SALMONELLE ATTENUEE CONTENANT UN PHAGE BERMUDES, David, G.; KING, Ivan, C.; CLAIRMONT, Caroline, A. VION PHARMACEUTICALS, INC.; BERMUDES, David, G.; KING, Ivan, C.; CLAIRMONT, Caroline, A. Patent NUMBER KIND DATE ____.

DESIGNATED STATES

DOCUMENT TYPE:

APPLICATION INFO.:

PRIORITY INFO.:

INVENTOR(S):

PATENT ASSIGNEE(S):

DOCUMENT TYPE:

PATENT INFORMATION:

DESIGNATED STATES W:

APPLICATION INFO.:

PRIORITY INFO.:

TITLE (ENGLISH):

PATENT ASSIGNEE(S):

PATENT INFORMATION:

TITLE (FRENCH):

INVENTOR(S):

L6 ANSWER 6 OF 6

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM

WO 2001014579 A2 20010301

TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG

APPLICATION INFO.: PRIORITY INFO.:

CI CM GA GN GW ML MR NE SN TD TG WO 2000-US23243 A 20000824 US 1999-60/150,928 19990826

=> d kwic 6

L6 ANSWER 6 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . the antiangiogenic 19 amino acid peptide fragment of Thrombospondin 1, the
anti-angiogenic 20
amino acid peptide fragment of SPARC, RGD and NGR containing
peptides, the small antiangiogenic peptides of laminin, fibronectin, procollagen and EGF, and
peptide antagonists
of integrin 43 and the VEGF. . .

gene

products can be co-delivered with cytokines, using the same or different promoters and optionally with an internal ribosome binding site. Similarly, a-1,3-galactosyl transferase expression on tumor cells allows complement-mediated cell killing.

=> d kwic 4

L6 ANSWER 4 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . the dpoptosis of angiogenic blood vessels (Brooks et al., 1994, Cell 79:1157-1164). Peptides comprising the RGD motif, and another integrin binding motif, NGR (amino acids Asn-Gln-Arg), showed markedly enhanced anti-tumor activity The inhibition of the activity of another type of cell surface receptor, namely the urokinase. . .

the anti]

angiogenic 22 amino acid peptide fragment of thrombospondin 1, the anti-angiogenic 20 amino acid peptide fragment of SPARC, RGD and NGR containing peptides, the small anti-angiogenic peptides of laminin, fibronectin, procollagen and EGF, and peptide antagonists of integrin 03 and the VEGF receptor.

Yet another immunomodulating agent is, a-1,3-galactosyl transferase, whose expression on tumor cells allows comple ment-mediated cell killing. Further, another immunomodulating agent is a tumor-associated antigen, i.e. a molecule. . .

CLMEN. . . the anti-angiogenic 22 amino acid peptide fragment of thrombospondin 1, the anti-angiogenic 20 amino acid peptide fragment of SPARC, RGD and NGR containing peptides, the small anti-angiogenic peptides of laminin, fibronectin, procollagen and EGF, and

peptide antagonists of integrin avP3, or VEGF receptor. anti-angiogenic 22 amino acid peptide fragment of Thrombospondin I, the anti-angiogenic 20 amino acid peptide fragment of SPARC, RGD and NGR containing peptides, the small anti-angiogenic peptides of laminin, fibronectin, procollagen and EGF, and peptide antagonists of integrin 043, or VEGF receptor. the anti-angiogenic 22 amino acid peptide fragment of thrombospondin 1, anti-angiogenic 20 amino acid peptide fragment of SPARC, RGD and NGR containing peptides, the small anti-angiogenic peptides of laminin, fibronectin, procollagen and EGF, and peptide antagonists of integrin avP3, or VEGF receptor. => d kwic 1 ANSWER 1 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN . . the apoptosis of angiogenic blood vessels (Brooks et al., 1994, Cell 79:1157-1164). Peptides comprising the RGD motif, and another integrin binding motif, NGR (amino acids Asn-Gln-Arg), showed markedly enhanced anti-tumor activity The inhibition of the activity of another type of cell surface receptor, namely the urokinase. receptor antagonists (Soker et aL, 1993] J. Biol. Chem. 272:31582-31588). In a highly preferred embodiment, the small peptide comprises an RGD or NGR motif. In certain modes of the embodiment, the RGD or NGR containing peptide is presented on the cell surface of the host bacteria, for example, by fusing the nucleic acid encoding the. for both CD28 and CTLA-4, can 1 5 also be delivered to enhance T cell mediated immunity. Yet another immunomodulating agent is a-1,3-galactosyl transferase

whose expression on tumor cells allows complementmediated cell killing. Moreover, certain antibodies can modulate the activity of different aspects of.

13.40, the anti-angiogenic 22 amino acid peptide fragment of thrombospondin 1, the anti-angiogenic 20 amino acid peptide fragment of SPARC, RGD and NGR containing peptides, the small anti-angiogenic peptides of laminin, fibronectin, procollagen and EGF, integrina, 03 antagonists (e.g., anti-integrin aA antibodies), acid fibroblast growth factor.

=> file caplus COST IN U.S. DOLLARS

L6

DETD

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http://www.cas.org/infopolicy.html

=> s NGR

420 NGR 14 NGRS

L7 432 NGR

(NGR OR NGRS)

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8843144 1 6695441 3

101240 GALACTOS?

L8 729 1 (W) 3 (W) GALACTOS?

=> s 17 (L) 18

L9 2 L7 (L) L8

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L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:902137 CAPLUS

DOCUMENT NUMBER: 141:374703

TITLE: Use of human serum albumin and NGR peptide

conjugates bearing α - 1,3-

galactose epitopes in targeting tumor

vasculature

INVENTOR(S): Wagner, Thomas E.; Yu, Xianzhang; Wei, Yanzhang

PATENT ASSIGNEE(S): Greenville Hospital System, USA

SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091551	A2	20041028	WO 2004-US9706	20040331
WO 2004091551	A3	20050217		

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             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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             TD, TG
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                                20050113
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                                20060111
                                             EP 2004-759057
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WO 2004-US9706 W 20040331
PRIORITY APPLN. INFO.:
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ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:202868 CAPLUS

DOCUMENT NUMBER:

141:235825

TITLE:

In vitro targeted killing of human endothelial cells

by co-incubation of human serum and NGR

peptide conjugated human albumin protein bearing

 α (1-3) galactose

epitopes

AUTHOR(S):

Holle, Lori; Song, Wendy; Hicks, Labri; Holle, Eric; Holmes, Lillian; Wei, Yanzhang; Li, Jinhua; Wagner,

Thomas; Yu, Xianzhong

CORPORATE SOURCE:

Greenville Hospital System, Oncology Research

Institute, Greenville, SC, 29605, USA Oncology Reports (2004), 11(3), 613-616

CODEN: OCRPEW; ISSN: 1021-335X

PUBLISHER:

SOURCE:

Oncology Reports

DOCUMENT TYPE:

Journal

LANGUAGE:

English

REFERENCE COUNT:

18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FULL ESTIMATED COST

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FILE LAST UPDATED:

25 SEP 2006

<20060925/UP>

MOST RECENT UPDATE WEEK:

200638

<200638/EW>

FILE COVERS 1978 TO DATE

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http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE (last updated April 10, 2006) <<<

>>> NEW PRICES IN PCTFULL AS OF 01 JULY 2006. FOR DETAILS, PLEASE SEE HELP COST <<<

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                 (WO1/PN)
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                 (WO1061017/PN)
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                 (WO2001061017/PN)
=> s 113 and albumin
         48356 ALBUMIN
          2492 ALBUMINS
         48908 ALBUMIN
                 (ALBUMIN OR ALBUMINS)
L14
             1 L13 AND ALBUMIN
=> d kwic
      ANSWER 1 OF 1
L14
                       PCTFULL COPYRIGHT 2006 Univentio on STN
PΙ
       WO 2001061017
                          A2 20010823
DETD . . . 0.5 M sodium chloride, 0.2 M glycine-HCI). The
       TNF-antigen containing fractions were neutralized and dialyzed against
       sterile physiological solution. Endotoxin-free human serum
       added before dialysis (0.5 mg/ml) to prevent protein adsorption on
       membranes. The TNF content in each fraction was measured by ELISA.
       Preliminary experiments showed that the anti-tumor activity was not
       changed by the addition of human serum albumin to TNF and
       solutions, as a carrier. Each experiment was carried out with 5 mice per
       group. The tumor growth was. . .
       competitors
       Competitor Binding of WM 1 5 to tumor
       associated vessels
       None +
       NGR-TNF (25 ]Lg/ml)
       NGR-IFNy (50 gg/ml)
       CNGRC (100 ]Lg/ml)
       TNF (25 gg/ml) +
       Human serum albumin (25 Rg/ml) +
       Synthetic CgA(60-68) (100 gg/ml) +
       ' The competitor, in PBS containing 2% BSA, was added in the blocking
       step and.
=> file caplus
COST IN U.S. DOLLARS
                                                 SINCE FILE
                                                                 TOTAL
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                                                               SESSION
FULL ESTIMATED COST
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FILE COVERS 1907 - 2 Oct 2006 VOL 145 ISS 15 FILE LAST UPDATED: 1 Oct 2006 (20061001/ED)

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=> s target?

L15 492221 TARGET?

=> d his

L1

(FILE 'HOME' ENTERED AT 11:01:59 ON 02 OCT 2006)

FILE 'PCTFULL' ENTERED AT 11:02:11 ON 02 OCT 2006 458 S NGR

L2 15772 S GALACTOSE

L3 56 S L1 AND L2

L4 379 S 1 () 3 () GALACTOS?

L5 8 S L4 AND L1

L6 6 S L5 NOT PY>2003

FILE 'CAPLUS' ENTERED AT 11:08:29 ON 02 OCT 2006

L7 432 S NGR

L8 729 S 1 () 3 () GALACTOS?

L9 2 S L7 (L) L8

FILE 'PCTFULL' ENTERED AT 11:09:19 ON 02 OCT 2006

L10 0 S WO 01/61017/PN

L11 0 S WO 0161017/PN L12 0 S WO 01061017/PN

1 S WO 2001061017/PN

L14 1 S L13 AND ALBUMIN

FILE 'CAPLUS' ENTERED AT 11:11:15 ON 02 OCT 2006 L15 492221 S TARGET?

=> s 115 and 18

L16 124 L15 AND L8

=> s 115 (L) 18

L17 102 L15 (L) L8

=> s albumin and 117

126728 ALBUMIN

84802 ALBUMINS

148598 ALBUMIN

(ALBUMIN OR ALBUMINS)

L18 5 ALBUMIN AND L17

=> d ibib 1-5

L18 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:902137 CAPLUS

DOCUMENT NUMBER: 141:374703

TITLE: Use of human serum albumin and NGR peptide

> conjugates bearing α - 1,3galactose epitopes in targeting

tumor vasculature

INVENTOR(S): Wagner, Thomas E.; Yu, Xianzhang; Wei, Yanzhang

PATENT ASSIGNEE(S): Greenville Hospital System, USA

SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.				KIND DA		DATE		APPLICATION NO.						DATE			
	WO 2004091551 WO 2004091551				A2 20041028 A3 20050217			WO 2004-US9706					20040331					
		W:	AE,	AG,	AL,			AU,		BA.	BB.	BG.	BR.	BW.	BY.	BZ.	.CA.	CH.
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				-	-			ID,					•	•			•	•
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		RW:						MW,										
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								HU,										
			SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,
			TD,	TG														
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	ΕP	1613	344	•		A2		2006	0111		EP 2	004-	7590	57		2	0040	331
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			ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	PL,	SK
PRIO	RITY	Z APP	LN.	INFO	. :					1	US 2	003-	4583	95P		P 2	0030	331
	WO 2004-US9706 W 20040331									331								

L18 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:202868 CAPLUS

DOCUMENT NUMBER: 141:235825

TITLE: In vitro targeted killing of human

endothelial cells by co-incubation of human serum and

NGR peptide conjugated human albumin protein

bearing α (1-3) galactose epitopes

Holle, Lori; Song, Wendy; Hicks, Labri; Holle, Eric; AUTHOR(S):

Holmes, Lillian; Wei, Yanzhang; Li, Jinhua; Wagner,

Thomas; Yu, Xianzhong

CORPORATE SOURCE: Greenville Hospital System, Oncology Research

Institute, Greenville, SC, 29605, USA Oncology Reports (2004), 11(3), 613-616

SOURCE: CODEN: OCRPEW; ISSN: 1021-335X

PUBLISHER: Oncology Reports

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:603778 CAPLUS

DOCUMENT NUMBER: 137:351246 TITLE: Elimination of anti-Gal B cells by α -gal ricin AUTHOR(S): Tanemura, Masahiro; Ogawa, Haruko; Yin, Deng-Ping;

Chen, Zhao-Chun; DiSesa, Verdi J.; Galili, Uri

CORPORATE SOURCE: Department of Cardiovascular-Thoracic Surgery, Rush

University, Chicago, IL, 60612, USA

SOURCE: Transplantation (2002), 73(12), 1859-1868

CODEN: TRPLAU; ISSN: 0041-1337 Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal LANGUAGE: English

PUBLISHER:

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:227313 CAPLUS

DOCUMENT NUMBER: 137:400

TITLE: Evaluation of Different α -Galactosyl

Glycoconjugates for Use in Xenotransplantation
AUTHOR(S): Byrne, Guerard W.; Schwarz, Alexander; Fesi, Joanna

R.; Birch, Patrick; Nepomich, Anna; Bakaj, Ivona; Velardo, Margaret A.; Jiang, Cong; Manzi, Adriana; Dintzis, Howard; Diamond, Lisa E.; Logan, John S.

CORPORATE SOURCE: Nextran Inc., Princeton, NJ, USA

SOURCE: Bioconjugate Chemistry (2002), 13(3), 571-581

CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:156401 CAPLUS

DOCUMENT NUMBER: 124:225167

TITLE: Macrophage targeting with technetium-99m labeled J001

acylated poly-galactoside for scintigraphy of

inflammation: optimization and assessment of imaging

specificity in experimental arthritis

AUTHOR(S): Miot-Noirault, E.; Perin, F.; Routledge, L.; Normier,

G.; Le Pape, A.

CORPORATE SOURCE: Laboratoire de Biophysique Cellulaire, Faculte de

Medecine, Tours, F-37032, Fr.

SOURCE: European Journal of Nuclear Medicine (1996), 23(1),

61-8

CODEN: EJNMD9; ISSN: 0340-6997

PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

=> d ibib abs kwic 1-5

L18 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:902137 CAPLUS

DOCUMENT NUMBER: 141:374703

TITLE: Use of human serum albumin and NGR peptide

conjugates bearing α - 1,3- galactose epitopes in targeting

tumor vasculature

INVENTOR(S): Wagner, Thomas E.; Yu, Xianzhang; Wei, Yanzhang

PATENT ASSIGNEE(S): Greenville Hospital System, USA

SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT:]

PATENT INFORMATION:

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PATENT NO.
                         KIND
                                  DATE
                                              APPLICATION NO.
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                          A2
                                              WO 2004-US9706
     WO 2004091551
                                  20041028
                                                                        20040331
     WO 2004091551
                           A3
                                  20050217
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             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
              NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
              TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
              BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
              ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
              SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
     CA 2521109
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                                               CA 2004-2521109
                                                                        20040331
     US 2005009740
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                                  20050113
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                                              EP 2004-759057
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              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK
PRIORITY APPLN. INFO.:
                                               US 2003-458395P
                                                                 P 20030331
                                                                    W 20040331
                                               WO 2004-US9706
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Use of human serum albumin and NGR peptide conjugates bearing AB α - 1,3-galactose epitopes in targeting tumor vasculature. The NGR/galactose- α 1,3-Gal-HSA peptide was designed to specifically target CD13 pos. cells and induce cell lysis. NGR is the targeting component of the peptide in that it binds the CD13 isoform (aminopeptidase) that is expressed in tumor vessels. Galactose .alpha.1,3galactose terminal carbohydrate epitope (α 1,3Gal) induces a strong antibody reaction in human and Old World Monkeys and in vivo, this reaction leads to organ rejection. The human serum albumin (HSA) bearing $\alpha 1$, 3Gal epitope was therefore used to lyse cells. $NGR/\alpha 1,3Gal-HSA$ binds CD13 pos. human umbilical vein endothelial cells (HUVEC). NGR/ α 1,3Gal-HSA induces lysis of HUVECs upon incubation with human serum. Therefore, by conjugating NGR to HSA bearing al, 3Gal epitopes, cells expressing CD13 could be lysed.

TI Use of human serum albumin and NGR peptide conjugates bearing $\alpha -$ 1,3-galactose epitopes in targeting tumor vasculature

AΒ Use of human serum albumin and NGR peptide conjugates bearing α - 1,3-galactose epitopes in targeting tumor vasculature. The NGR/galactose- α 1,3-Gal-HSA peptide was designed to specifically target CD13 pos. cells and induce cell lysis. NGR is the targeting component of the peptide in that it binds the CD13 isoform (aminopeptidase) that is expressed in tumor vessels. Galactose .alpha.1,3galactose terminal carbohydrate epitope (α 1,3Gal) induces a strong antibody reaction in human and Old World Monkeys and in vivo, this reaction leads to organ rejection. The human serum albumin (HSA) bearing $\alpha 1,3Gal$ epitope was therefore used to lyse cells. $NGR/\alpha 1,3Gal-HSA$ binds CD13 pos. human umbilical vein endothelial cells (HUVEC). NGR/ α 1,3Gal-HSA induces lysis of HUVECs upon incubation with human serum. Therefore, by conjugating NGR to HSA bearing α 1,3Gal epitopes, cells expressing CD13 could be lysed.

ST NGR peptide human serum albumin galactose epitope conjugate angiogenesis

IT Complement

RL: BSU (Biological study, unclassified); BIOL (Biological study) (-mediated hyperactive immune response; use of human serum

```
albumin and NGR peptide conjugates bearing \alpha- 1,
        3-galactose epitopes in targeting tumor
        vasculature)
ΙT
     Peptides, biological studies
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (NGR; use of human serum albumin and NGR peptide conjugates
        bearing \alpha- 1,3-galactose epitopes in
        targeting tumor vasculature)
IT
     Intestine, neoplasm
        (colorectal; use of human serum albumin and NGR peptide
        conjugates bearing \alpha- 1,3-galactose
        epitopes in targeting tumor vasculature)
IT
    Neoplasm
    Neoplasm
        (head and neck; use of human serum albumin and NGR peptide
        conjugates bearing \alpha- 1,3-galactose
        epitopes in targeting tumor vasculature)
IT
     Drug delivery systems
        (injections, i.v.; use of human serum albumin and NGR peptide
        conjugates bearing \alpha- 1,3-galactose
        epitopes in targeting tumor vasculature)
ΙT
    Antibodies and Immunoglobulins
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (monoclonal, .alpha.1, 3-galactose; use of
        human serum albumin and NGR peptide conjugates bearing
        \alpha- 1,3-galactose epitopes in
        targeting tumor vasculature)
     Albumins, biological studies
ΙT
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (serum; use of human serum albumin and NGR peptide conjugates
        bearing \alpha- 1,3-galactose epitopes in
        targeting tumor vasculature)
ΙT
    Vein
        (umbilical, endothelium; use of human serum albumin and NGR
        peptide conjugates bearing \alpha- 1,3-
        galactose epitopes in targeting tumor vasculature)
IT
     Immunity
     Neoplasm
        (use of human serum albumin and NGR peptide conjugates
        bearing -1,3-galactose epitopes in
        targeting tumor vasculature)
IT
    Angiogenesis inhibitors
    Animal cell
    Animal tissue
    Antitumor agents
     Bladder, neoplasm
     Brain, neoplasm
     Cytolysis
     Drug delivery systems
     Head and Neck, neoplasm
     Head and Neck, neoplasm
     Human
     Kidney, neoplasm
     Lung, neoplasm
    Mammary gland, neoplasm
    Ovary, neoplasm
     Pancreas, neoplasm
     Prostate gland, neoplasm
        (use of human serum albumin and NGR peptide conjugates
        bearing \alpha- 1,3-galactose epitopes in
        targeting tumor vasculature)
IT
     Ligands
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (use of human serum albumin and NGR peptide conjugates
        bearing \alpha- 1,3-galactose epitopes in
        targeting tumor vasculature)
IΤ
     Antibodies and Immunoglobulins
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (.alpha.1,3-galactose; use of human serum
        albumin and NGR peptide conjugates bearing \alpha- 1,
        3-galactose epitopes in targeting tumor
        vasculature)
IT
     59-23-4, Galactose, biological studies
                                              13168-24-6, Galactose \alpha-
     1,3-galactose
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (galactose .alpha.1,3-galactose antibody;
        use of human serum albumin and NGR peptide conjugates bearing
        \alpha- 1,3-galactose epitopes in
        targeting tumor vasculature)
L18 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                         2004:202868 CAPLUS
DOCUMENT NUMBER:
                         141:235825
TITLE:
                          In vitro targeted killing of human
                          endothelial cells by co-incubation of human serum and
                         NGR peptide conjugated human albumin protein
                         bearing \alpha (1-3)
                          galactose epitopes
AUTHOR(S):
                         Holle, Lori; Song, Wendy; Hicks, Labri; Holle, Eric;
                         Holmes, Lillian; Wei, Yanzhang; Li, Jinhua; Wagner,
                          Thomas; Yu, Xianzhong
                         Greenville Hospital System, Oncology Research
CORPORATE SOURCE:
                          Institute, Greenville, SC, 29605, USA
SOURCE:
                          Oncology Reports (2004), 11(3), 613-616
                          CODEN: OCRPEW; ISSN: 1021-335X
PUBLISHER:
                         Oncology Reports
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
     The NGR/\alpha1, 3Gal-HSA peptide was designed to specifically
     target CD13 pos. cells and induce cell lysis. NGR is the
     targeting component of the peptide in that it binds the CD13
     isoform (aminopeptidase) that is expressed in tumor vessels. Galactose
     .alpha.1,3-galactose terminal carbohydrate
     epitope (\alpha1,3Gal) induces a strong antibody reaction in human and
     Old World Monkeys and in vivo, this reaction leads to organ rejection.
     The human serum albumin (HSA) bearing \alpha1,3Gal epitope was
     therefore used to lyse cells. In the present study, we were able to
     demonstrate that NGR/\alpha 1, 3Gal-HSA binds CD13 pos. human umbilical
     vein endothelial cells (HUVEC). We also found by live/dead fluorescent
     staining that NGR/\alpha 1, 3Gal-HSA was able to induce lysis of HUVECs
     upon incubation with human serum. Therefore, by conjugating NGR to HSA
     bearing \alpha 1, 3Gal epitopes, we are able to specifically target
     and lyse cells expressing CD13. This strategy may be potentially useful
     in tumor anti-angiogenesis therapy.
REFERENCE COUNT:
                         18
                                THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
     In vitro targeted killing of human endothelial cells by
ΤI
     co-incubation of human serum and NGR peptide conjugated human
     albumin protein bearing \alpha (1-3)
     galactose epitopes
AB
     The NGR/\alpha1,3Gal-HSA peptide was designed to specifically
     target CD13 pos. cells and induce cell lysis. NGR is the
     targeting component of the peptide in that it binds the CD13
     isoform (aminopeptidase) that is expressed in tumor vessels.
```

.alpha.1,3-galactose terminal carbohydrate

epitope (α 1,3Gal) induces a strong antibody reaction in human and Old World Monkeys and in vivo, this reaction leads to organ rejection. The human serum albumin (HSA) bearing α 1,3Gal epitope was therefore used to lyse cells. In the present study, we were able to demonstrate that NGR/ α 1,3Gal-HSA binds CD13 pos. human umbilical vein endothelial cells (HUVEC). We also found by live/dead fluorescent staining that NGR/ α 1,3Gal-HSA was able to induce lysis of HUVECs upon incubation with human serum. Therefore, by conjugating NGR to HSA bearing α 1,3Gal epitopes, we are able to specifically target and lyse cells expressing CD13. This strategy may be potentially useful in tumor anti-angiogenesis therapy.

- ST NGR peptide human serum albumin galactose epitope conjugate angiogenesis
- IT Angiogenesis inhibitors Cytolysis Drug delivery systėms Human

(CD13 pos. HUVEC cells were lysed with coincubation of human serum albumin and NGR peptide bearing galactose $\alpha 1,3$ -galactose epitope in vitro indicating NGR/ $\alpha 1,3$ Gal-HSA possible use in tumor anti-angiogenesis therapy)

IT Protein motifs

(NGR; CD13 pos. HUVEC cells were lysed with coincubation of human serum albumin and NGR peptide bearing galactose $\alpha 1,3$ -galactose epitope in vitro indicating NGR/ $\alpha 1,3$ Gal-HSA possible use in tumor anti-angiogenesis therapy)

IT Albumins, biological studies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(serum; CD13 pos. HUVEC cells were lysed with coincubation of human serum albumin and NGR peptide bearing galactose $\alpha 1,3$ -galactose epitope in vitro indicating NGR/ $\alpha 1,3$ Gal-HSA possible use in tumor anti-angiogenesis therapy)

IT Endothelium

(umbilical venous; CD13 pos. HUVEC cells were lysed with coincubation of human serum albumin and NGR peptide bearing galactose $\alpha 1,3$ -galactose epitope in vitro indicating NGR/ $\alpha 1,3$ Gal-HSA possible use in tumor anti-angiogenesis therapy)

IT Vein

IΤ

(umbilical, endothelium; CD13 pos. HUVEC cells were lysed with coincubation of human serum albumin and NGR peptide bearing galactose $\alpha 1, 3$ -galactose epitope in vitro indicating NGR/ $\alpha 1, 3$ Gal-HSA possible use in tumor anti-angiogenesis therapy) Antibodies and Immunoglobulins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (α 1,3-galactose; CD13 pos. HUVEC cells were lysed with coincubation of human serum albumin and NGR peptide bearing galactose α 1,3-galactose epitope in vitro indicating NGR/ α 1,3Gal-HSA possible use in tumor anti-angiogenesis therapy)

IT 9054-63-1, CD13

RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD13 pos. HUVEC cells were lysed with coincubation of human serum albumin and NGR peptide bearing galactose α 1,3-galactose epitope in vitro indicating NGR/ α 1,3Gal-HSA possible use in tumor anti-angiogenesis therapy)

IT 59-23-4, Galactose, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study) (galactose $\alpha 1,3$ -galactose antibody; CD13 pos. HUVEC cells were lysed with coincubation of human serum albumin and NGR peptide bearing galactose $\alpha 1,3$ -galactose epitope in vitro)

L18 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN ACCESSION NUMBER: 2002:603778 CAPLUS DOCUMENT NUMBER: 137:351246

TITLE: AUTHOR(S):

CORPORATE SOURCE:

Elimination of anti-Gal B cells by α -gal ricin Tanemura, Masahiro; Ogawa, Haruko; Yin, Deng-Ping; Chen, Zhao-Chun; DiSesa, Verdi J.; Galili, Uri Department of Cardiovascular-Thoracic Surgery, Rush

University, Chicago, IL, 60612, USA

SOURCE: Transplantation (2002), 73(12), 1859-1868

CODEN: TRPLAU; ISSN: 0041-1337 Lippincott Williams & Wilkins

PUBLISHER: Lippince
DOCUMENT TYPE: Journal
LANGUAGE: English

Background. A major barrier in pig to human organ transplantation is the binding of human anti-Gal to α -gal epitopes (Gal α 1-3Gal β 1-4GlcNAc-R) on pig cells, resulting in hyperacute and acute vascular rejection of pig xenografts. Moreover, the immune system in xenograft recipients is activated by these epitopes to produce high affinity anti-Gal, which is also detrimental to xenografts. Production of anti-Gal can be prevented by specific elimination of anti-Gal B cells. This was achieved with the toxin ricin A, coupled to human $\alpha 1$ -acidglycoprotein modified to carry α -gal epitopes. This complex, designated α -gal ricin, is targeted in vivo to anti-Gal B cells by interaction with the Ig mols. (i.e., B cell receptors) on these cells. Methods, Carbohydrate chains on α 1-acid glycoprotein were converted to carry α -gal epitopes by enzymic treatment with recombinant .alpha.1,3 galactosyltransferase $(\alpha 1, 3GT)$. This mol. and ricin A were biotinylated and coupled by avidin to generate α -gal ricin. The efficacy of α -gal ricin in eliminating anti-Gal B cells was studied in the exptl. model of α 1,3GT knockout (KO) mice. These mice produce large amts. of anti-Gal IgG when immunized with pig kidney membranes, as measured by ELISA with α -gal epitopes linked to bovine serum albumin (BSA). In the absence of anti-Gal B cells, these mice lack the ability to produce anti-Gal. Results. Repeated administration of α -gal ricin into $\alpha 1,3GT$ KO mice resulted in elimination of anti-Gal B cells, thereby preventing production of anti-Gal IgG after immunization with pig kidney membranes. This prevention of anti-Gal production occurred with doses of $\alpha\text{-gal}$ ricin that were not toxic to the mice and did not affect production of antibodies with other specificities. Conclusions. Administration of α -gal ricin results in specific elimination of anti-Gal B cells in $\alpha 1,3 \text{GT}$ KO mice. The elimination of these B cells may prove to be helpful in attempts to achieve immune tolerance to α -gal epitopes in primates.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Background. A major barrier in pig to human organ transplantation is the AΒ binding of human anti-Gal to α -gal epitopes (Gal α 1-3Gal β 1-4GlcNAc-R) on pig cells, resulting in hyperacute and acute vascular rejection of pig xenografts. Moreover, the immune system in xenograft recipients is activated by these epitopes to produce high affinity anti-Gal, which is also detrimental to xenografts. Production of anti-Gal can be prevented by specific elimination of anti-Gal B cells. This was achieved with the toxin ricin A, coupled to human $\alpha 1$ -acid glycoprotein modified to carry α -gal epitopes. This complex, designated α -gal ricin, is targeted in vivo to anti-Gal B cells by interaction with the Ig mols. (i.e., B cell receptors) on these cells. Methods. Carbohydrate chains on α 1-acid glycoprotein were converted to carry α -gal epitopes by enzymic treatment with recombinant .alpha.1,3 galactosyltransferase $(\alpha 1, 3GT)$. This mol. and ricin A were biotinylated and coupled by avidin to generate α -gal ricin. The efficacy of α -gal ricin in eliminating anti-Gal B cells was studied in the exptl. model of α 1,3GT knockout (KO) mice. These mice produce large amts. of anti-Gal IgG when immunized with pig kidney membranes, as measured by ELISA with $\alpha\text{-gal}$ epitopes linked to bovine serum $% \left(1\right) =\left(1\right) +\left(1$ (BSA). In the absence of anti-Gal B cells, these mice lack the ability to

produce anti-Gal. Results. Repeated administration of α -gal ricin into $\alpha 1,3GT$ KO mice resulted in elimination of anti-Gal B cells, thereby preventing production of anti-Gal IgG after immunization with pig kidney membranes. This prevention of anti-Gal production occurred with doses of α -gal ricin that were not toxic to the mice and did not affect production of antibodies with other specificities. Conclusions. Administration of α -gal ricin results in specific elimination of anti-Gal B cells in $\alpha 1,3GT$ KO mice. The elimination of these B cells may prove to be helpful in attempts to achieve immune tolerance to α -gal epitopes in primates.

L18 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:227313 CAPLUS

DOCUMENT NUMBER: 137:400

TITLE: Evaluation of Different α-Galactosyl

Glycoconjugates for Use in Xenotransplantation

AUTHOR(S): Byrne, Guerard W.; Schwarz, Alexander; Fesi, Joanna

R.; Birch, Patrick; Nepomich, Anna; Bakaj, Ivona; Velardo, Margaret A.; Jiang, Cong; Manzi, Adriana; Dintzis, Howard; Diamond, Lisa E.; Logan, John S.

CORPORATE SOURCE: Nextran Inc., Princeton, NJ, USA

SOURCE: Bioconjugate Chemistry (2002), 13(3), 571-581

CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

AΒ Porcine organs are rapidly rejected after transplantation into primate recipients due to the presence of preexisting Igs that bind to terminal galactose .alpha.1,3 galactose residues $(\alpha$ -galactosyl) present on porcine glycoproteins and glycolipids. Currently available immunosuppressive reagents have been largely ineffective at controlling the synthesis of these anti-Gal antibodies. Nonantigenic hapten polymers have been shown to be effective materials for blocking humoral immune responses in various model systems. We have developed a series of α -galactosyl glycoconjugate polymers and tested their ability to block anti-Gal antibody binding in vitro and in vivo. A galactose .alpha.1,3 galactose β 1,4 GlcNAc trisaccharide free acid (TRFA) with a hexanoic acid spacer, containing five methylene groups and a carboxylic acid, was produced and coupled to a variety of polymeric backbones including dextran, branched poly(ethylene glycol) (PEG), and poly-L-lysine. The ability of monomeric TRFA and the α -galactosyl conjugates to block anti-Gal IgG and IgM binding was determined using a competition ELISA assay on defined HSA-Gal glycoconjugates and porcine microvascular endothelial cell substrates. We show that branched PEG carriers, with a TRFA sugar attached to each branch, exhibit enhanced antibody blocking ability

compared to TRFA, but at higher target antigen densities these simple PEG conjugates are no more effective then an equivalent amount of TRFA in

blocking anti-Gal IgM antibody interactions. In contrast, polymers of the branched PEG conjugates and linear conjugates made using dextran and poly-L-lysine were 2000 to 70000-fold more effective inhibitors of anti-Gal antibodies. In a study using nonhuman primates, a single dose infusion of polymeric PEG or dextran glycoconjugates dramatically reduced the level of circulating anti-Gal antibodies in cynomolgus monkeys for at least 72 h. Glycoconjugates similar to these might be useful both to block anti-Gal interactions in vivo and to specifically control the induced anti-Gal immune response.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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IT Albumins, biological studies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(serum, human, glycoconjugates; evaluation of different α -galactosyl glycoconjugates for use in xenotransplantation)

L18 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:156401 CAPLUS

DOCUMENT NUMBER: 124:225167

TITLE: Macrophage targeting with technetium-99m labeled J001

acylated poly-galactoside for scintigraphy of

inflammation: optimization and assessment of imaging

specificity in experimental arthritis

AUTHOR(S): Miot-Noirault, E.; Perin, F.; Routledge, L.; Normier,

G.; Le Pape, A.

CORPORATE SOURCE: Laboratoire de Biophysique Cellulaire, Faculte de

Medecine, Tours, F-37032, Fr.

SOURCE: European Journal of Nuclear Medicine (1996), 23(1),

61-8

CODEN: EJNMD9; ISSN: 0340-6997

PUBLISHER: Springer DOCUMENT TYPE: Journal LANGUAGE: English

AB J001, an acylated poly-(1,3)-galactoside purified from the membrane of Klebsiella pneumoniae, assocs. selectively with macrophages via the binding to CD11b and CD14 mols. Inflammatory foci known to recruit macrophages could thus be imaged with technetium-99m labeled J001. This study aims to define the optimal scintigraphic protocol for 99mTc-J001 imaging and to evaluate the specificity of J001 scans. A dose range study was conducted in rabbits with immunol. arthritis using six different specific activities ranging from 370 to 11840 MBq·mg-1 while the i.v. injected activity was constant (37 MBq). Radiochem. purity for each preparation was documented together with the in vivo stability of the 99mTc-J001 complex using exclusion-diffusion radio-HPLC of serum collected 1 h after radiopharmaceutical administration. Scintigraphic images were recorded at 2, 3 and 4 h and

analyzed using indexes calculated from regions of interest. Specificity of the macrophage imaging was assessed by comparison with scans obtained after administration of 99mTcO4- or 99mTc-albumin nanocolloids. A protocol of plasma transfusion was also used to inject 99mTc-J001 after complete removal of radioactive colloids likely to be generated during the labeling. For the higher specific activities (5920 and 11840 MBq·mg-1), radiochem. purity degradation and in vitro 99mTc transchelation were noted. To prevent transchelation and 99mTc bond hydrolysis likely to impair imaging specificity, 1480 MBq·mg-1 corresponding to 25 μg injected J001 was found to be the optimal usable specific activity. Results obtained with the various tracers support the hypothesis that macrophage targeting is the main factor involved in the J001 imaging of arthritis.

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=> d his

L14

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L2
L3
             56 S L1 AND L2
            379 S 1 () 3 () GALACTOS?
L4
L5
              8 S L4 AND L1
L6
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L8
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L9
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L10
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L11
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              0 S WO 01061017/PN
L12
L13
             1 S WO 2001061017/PN
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1 S L13 AND ALBUMIN

FILE 'CAPLUS' ENTERED AT 11:11:15 ON 02 OCT 2006 L15 492221 S TARGET? L16 124 S L15 AND L8 L17 102 S L15 (L) L8 5 S ALBUMIN AND L17

=> file dissab

L18

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=> s 1 () 3 () galactos?

373994 1

297830 3

3250 GALACTOS?

L19 32 1 (W) 3 (W) GALACTOS?

=> s NGR and 119

17 NGR

L20 0 NGR AND L19

=> s RGD and 119

275 RGD

45 RGDS

307 RGD

(RGD OR RGDS)

L21

0 RGD AND L19

=> s albumin and 119

3183 ALBUMIN

101 ALBUMINS

3236 ALBUMIN

(ALBUMIN OR ALBUMINS)

L22

0 ALBUMIN AND L19

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) .	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY 0.00	SESSION -3.75

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